REMARKS/ARGUMENTS

Claims 119-126 and 129-131 are pending in this application. The rejections to the presently pending claims are respectfully traversed.

Claim Rejections – 35 U.S.C. §101 and §112 - First Paragraph

Claims 119-126 and 129-131 stand rejected under 35 U.S.C. §101 because, allegedly, "the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility." (Page 2 of the instant Final Office Action).

The Examiner maintains that "the PRO1097 gene has not been associated with tumor formation or development of cancer.....all that the specification does is present evidence that the DNA encoding PRO1097 is amplified in small number of samples" (Page 5 of the instant Final Final Office Action). The Examiner has relied on the teachings of Pennica *et al.* and Hu *et al.*, to allege that, strong opposing evidence exists regarding the prediction of protein expression from corresponding mRNA levels. The Examiner further relies on the teachings of Bieche *et al.* and Pitti *et al.* to allege that these authors did not use their data for diagnostic purposes, as in the instant application.

Applicants have discussed the references Pennica *et al.*, Bieche *et al.*, Pitti *et al.* and Hu *et al.*, in great detail in their Response dated January 5, 2007, and maintain their position regarding this matter. Applicants maintain that references Bieche *et al.* and Pitti *et al.* were presented to show the use of pooled DNA from normal, healthy donors as control was well-known and was widely utilized at the time of filing of the instant application. That the Bieche *et al.* and Pitti *et al.* used such controls for experimental purposes (and not for diagnostics, according to the Examiner) should bear no consequence to the fact that, pooled DNA controls were an acceptable control in the art at that time of filing of the instant application. Accordingly, the Examiner has not presented valid arguments or contrary evidence to show that the pooled control was not acceptable at the time of filing. Such a rejection is therefore improper.

The Examiner maintains that "the specification provides data purportedly showing a slight increase in DNA copy number in two different types of tumor tissue (lung and colon) of PRO1097" and further alleges that "gene amplification does not reliably correlate with polypeptide over-expression." The Examiner acknowledges that PRO1097 is novel but alleges

"it is not known whether PRO1097 is expressed in corresponding normal tissues and what the relative levels of expression are." The Examiner adds that she "cannot find any reason to suspect, that the protein encoded by the PRO1097 gene would confer any selective advantage on a cell expressing it" and that "the instant specification does not teach structure/ function analysis." (Page 3 of the instant Final Office Action).

Using this PCR-based assay, Appellants has made the assertion that the gene encoding for PRO1097 was significantly amplified. The Declaration by Dr. Audrey Goddard explains that a gene identified as being amplified at least 2-fold by the disclosed gene amplification assay in a tumor sample, relative to a normal sample, is useful as a marker for the diagnosis of cancer, and for monitoring cancer development and/or for measuring the efficacy of cancer therapy. The Examiner requests "structure/ function data" but this is not a requirement for the utility requirement. Similarly, a showing of a mechanism of action is also not a utility requirement. Applicants note that selective advantage to cell survival is not the only mechanism by which genes impact cancer, and for this additional reason, such a requirement is a heightened standard imposed by the Examiner. The premise for each of these rejections is improper according to the Utility standards set by the USPTO.

Instead, Applicants maintain that the specification, as filed, provides sufficient disclosure to establish a specific, substantial and credible utility for the PRO1097 polypeptide of SEQ ID NO:349 and that the increase in gene amplification for the DNA encoding PRO1097 is sufficient to confer patentable utility to the instantly claimed PRO1097 polypeptides, for the reasons presented throughout the prosecution of this application. For instance, Example 170 explicitly states that the PRO1097 DNA is significantly overexpressed in lung or colon tumors as compared to the normal control. Applicants add that the gene amplification data clearly supports a role for PRO1097 as a lung or colon tumor marker.

As discussed previously, it is not a legal requirement to establish a "necessary" correlation between an increase in gene copy number and protein expression levels or to find evidence that protein levels can be accurately predicted from gene amplification data. Instead, as discussed before, the evidentiary standard to be used throughout *ex parte* examination of a patent application is a preponderance of the totality of the evidence under consideration. Accordingly, the question is rather if it is more likely than not that a person of ordinary skill in the pertinent art

would recognize such a positive correlation between gene amplification levels and protein levels. Applicants respectfully submit that when the proper evidentiary standard is applied, a correlation must be acknowledged.

Applicants further maintain that, both Polakis Declarations (Polakis I and II) and the teachings in the art, represented by the more than 100 references presented in the IDS of July 5, 2006, support Applicants' assertion, in general, that changes in mRNA level generally lead to corresponding changes in the level of the expressed protein. Applicants submit that considering the evidence as a whole, with the overwhelming majority of the evidence supporting Applicants' asserted utility, a person of skill in the art would conclude that Applicants' asserted utility is "more likely than not true." *Id.*

Moreover, Applicants would like to bring to the Examiner's attention a recent decision by the Board of Patent Appeals and Interferences (Decision on Appeal No. 2006-1469). In its decision, the Board reversed the utility rejection, acknowledging that "there is a strong correlation between mRNA levels and protein expression." Applicants submit that, in the instant application, the Examiner has likewise not presented any evidence specific to the PRO1097 polypeptide to refute Applicants' assertion of a correlation between mRNA levels and protein expression.

Therefore, Applicants request that the Examiner reconsider this rejection and maintain that they have demonstrated utility for the PRO1097 polypeptide. Accordingly, the present 35 U.S.C. §101 and §112, first paragraph, utility rejections should be withdrawn.

Claim Rejections - 35 U.S.C. §112, First Paragraph - Enablement

Claims 119-126 and 129-131 stand further rejected under 35 U.S.C. §112, first paragraph, as allegedly "the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." (Pages 2-3 of the instant Final Office Action).

Applicants respectfully traverse this rejection. Based on the discussions throughout prosecution and above, under utility, for the PRO1097 protein in the diagnosis of lung or colon

cancer, Applicants submit that the skilled artisan would not require undue experimentation to make and use the claimed invention.

Accordingly, Applicants request that this rejection be withdrawn.

Claim Rejections - 35 U.S.C. §112, First Paragraph - Written Description

Claims 119-123 are also rejected under 35 U.S.C. §112, first paragraph because, according to Examiner, the subject matter was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention." (Page 10 of the instant Final Office Action).

Applicants respectfully traverse this rejection to the pending claims. Applicants have discussed the claim rejections in great detail in their Response dated January 5, 2007 and maintain their position regarding this matter. Accordingly, Applicants request that this rejection be withdrawn.

CONCLUSION

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (referencing Attorney's Docket No. **39780-2730 P1C29**).

Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: July 23, 2007

By:_____
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